PREFACE

Scene setting and objectives

Filarial infections represent a continuum of vector borne diseases and are responsible for substantial morbidity in human beings. There are at present no safe and effective chemotherapeutic agents which can kill the adult filarial worms and do not cause side effects in the mammalian host. The only chemotherapeutic treatments are diethylcarbamazine and ivermectin which are effective only at the larval stages i.e. microfilariae. This problem is enhanced by the emerging evidence that parasites are acquiring resistance to ivermectin and that there is increased resistance of vectors to insecticides. Therefore, there is an urgent need to develop new and effective macrofilaricidal agents.

Certain aspects, like carbohydrate and folate metabolism of filarial worms have been studied in detail and have been targeted on the basis of differences among the properties of key metabolic enzymes or functional pathways from their counterparts from mammalian hosts. Although most of the currently available drugs have been found to interfere with such metabolism but still these targets are unable to provide an ideal macrofilaricidal and side effect free drug. We here intend to try a preliminary evaluation of target attractiveness within the area of thiol-dependent parasitic antioxidant defence. Glutathione metabolism represents a prospective target for the antifilarial drug design. Glutathione (GSH) has been identified as an important part of the antioxidant system of filariids. The enzymes involved in the synthesis and degradation of GSH therefore deserve interest. All the normal mammalian cells have a considerable amount of GSH whereas filarial worms in contrast may have GSH concentrations close to that required for their survival, therefore, a little manipulation in glutathione metabolism of filarial worms may have drastic consequences. Present work involves the studies on γ-glutamyl cycle enzymes of filarial worms and the assessment of GSH depletion in filarial worms as a strategy in the development of new antifilarial drug.